REMARKS

New claim 28 has been added.

Non-obviousness

The Examiner has rejected claim 26 as being obvious over Webster et al. (WO 99/12543) and Godfrey (GB 2,173,499). Reconsideration and withdrawal of this rejection is respectfully requested having regard to the following comments.

The Examiner's relies on the cases of *In re Lemin*, *National Distillers*, *In re Susi*, and *Merck v. Biocraft* to assert that a prior art disclosure of a genus of useful compounds is sufficient to render *prima facie* obvious a species falling within the genus. The Applicant respectfully submits that more recent Federal Circuit jurisprudence has established that the fact a claimed species is encompassed by a prior art genus is not sufficient by itself to establish obviousness. See for example *In re Baird*, F.3d 380, 382 (Fed. Cir. 1994) which found that "[t]he fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious". See also *In re Jones*, 958 F.2d 347, 350 (Fed Cir. 1992) which "decline[d] to extract from *Merck v. Biocraft* the rule...that regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it". In other words, obviousness must be decided on a case-by-case basis.

As understood, the Examiner is citing Webster et al. and Godfrey individually against claim 26 and is acknowledging that neither reference expressly discloses the 14 specific compounds claimed in claim 26. MPEP 2144.08 addresses obviousness when prior art teaches a genus, and in particular sets out the following five factors to consider when determining whether one of ordinary skill in the art would have been motivated to select the claimed species.

(A) Size of the genus

The genuses disclosed by Webster et al. and Godfrey each encompass a nearly infinite number of diverse compounds. Notably, each of the variable groups in these genuses are characterized as substituted or unsubstituted (or optionally substituted), with no limit on the type of substitution, and furthermore are unlimited with respect to carbon chain length. The present circumstances are analogous to *In re Baird* (genus estimated to encompass more than 100 million different compounds) and to *In re Jones* (genus encompassed potentially infinite

number of compounds) and are distinguishable from *Merck v. Biocraft* cited by the Examiner (genus estimated to encompass only 1200 different compounds).

(B) Express teachings

In the *Merck v. Biocraft* case cited by the Examiner, the Court held that claims directed to diuretic compositions comprising a specific mixture of amiloride and hydrochlorothiazide were obvious over a prior art reference expressly teaching that amiloride was a pyrazinoylguanidine which could be coadministered with potassium excreting diuretic agents, including hydrochlorothiazide which was named as an example, to produce a diuretic composition. In contrast, in the present case neither Webster et al. nor Godfrey expressly teach any particular reason to select the X and Z substitutions found in the 14 compounds listed in claim 26.

(C) Teachings of structural similarity

MPEP 2144.08 indicates that, generally, some teaching of a structural similarity is necessary to suggest selection of the claimed species. Here, there are no such teachings, as discussed below.

Webster et al. discloses:

- A genus at Figure 1 and claim 1. This genus includes the compounds in present claim 26, but as discussed above is extremely broad and encompasses a nearly infinite number of diverse compounds.
- Two subgenuses at dependent claims 4 and 7. Since these are the only subgenuses taught by Webster et al., the Applicant submits that it would be reasonable to infer that these are preferred subgenuses. These subgenuses do not encompass 14 claimed compounds of present claim 26 and thus teach away from the present invention: *In re Baird*, 383. The subgenuses teach H or methyl as the X substituent, whereas the claimed compounds recite 2,4-dimethoxy-phenyl as the X substituent. H and methyl differ significantly in size and shape from 2,4-dimethoxy-phenyl, and these differences would be reasonably expected to confer different physical and chemical properties on the overall compound. The most specific subgenus (claim 7 of Webster et al.) teaches straight or branched carbon chains at the Z substituent. In contrast, the Z substituents of present claim 26 compounds of the present invention are cyclic and polycyclic groups. The difference between acyclic and cyclic structures have been held to render claimed compounds unobvious over prior art compounds. For example, in *In re Jones*, the Federal Circuit reversed an obviousness

rejection of a claimed compound with an acyclic structure where the prior art genus encompassed the claimed compound but the disclosed examples had dissimilar structures for example by being cyclic.

- Three specific dithiolopyrrolones at page 10 (code named XN0, XN1, and XN3). Since these are the only examples of specific dithiolopyrrolone compounds taught by Webster et al., the Applicant submits that it would be reasonable to infer that these are preferred species. The disclosed species have a methyl as the X substituent, whereas the claimed compounds recite 2,4-dimethoxy-phenyl as the X substituent. Again, methyl differs significantly in size and shape from 2,4-dimethoxy-phenyl. The disclosed species have methyl, straight carbon chain, or branched carbon chain as the Z substituent, whereas the Z substituents of the presently claimed compounds are cyclic or polycyclic. Again, the difference between acyclic and cyclic structures have been held to render claimed compounds unobvious over prior art compounds: *In re Jones*.

Godfrey discloses:

- The genus of Formula (I). This genus includes the compounds in present claim 26, but as discussed above is extremely broad and encompasses a nearly infinite number of diverse compounds.
- The specific compounds listed in Table 1. None of the X substituents listed in Table 1 bear a sufficient structural resemblance to the 2,4-dimethoxy-phenyl X substituent of present claim 26, and none of the Z substituents listed in Table 1 bear a sufficient structural resemblance to the cyclic Z substituents of present claim 26, to warrant a conclusion of obviousness. In *In re Susi* cited by the Examiner, a conclusion of obviousness was made because the difference between the claimed invention and a particularly preferred subgenus of the prior art was merely a hydroxyl group. The differences between the Table 1 compounds and the presently claimed compounds are clearly more significant than the presence or absence of one hydroxyl group.
- The subgenuses at dependent claims 5-8 are narrower than the genus of Formula (I) and include the presently claimed compounds but still encompass a nearly infinite number of diverse compounds.

The threshold for a finding of structural similarity sufficient to justify a conclusion of obviousness is high. According to the jurisprudence, obviousness is found where the similarity is "very close" and usually when the difference between the claimed invention and

prior art relates to a single difference in structure between the compounds or relates to a difference between isomers: tetra-orthoester versus tri-orthoester in *Dillon*, 919 F.2d at 692-693; replacement of an unsaturated carbon with a nitrogen atom in *In re Merck & Co.*, 800 F.2d 1091 at 1096-1097; omission of a methyl group from pyrazole ring in *In re Druey*, 319 F.2d 237 at 240; adjacent homologs and structural isomers in *In re Wilder*, 563 F.2d 457 at 460; and stereroisomers in *In re May*, 574 F.2d 1092 at 1093-1095. In the present case, neither Webster et al. nor Godfrey expressly disclose any substituents that differ from the X or Z substituents of the compounds in claim 26 by a single difference in structure or by an isomerism difference, let alone expressly disclose any of the X or Z substituents of the compounds in claim 26 themselves.

(D) Teachings of similar properties or uses
Webster et al. teaches use of the disclosed compounds as antineoplastic agents, which is a similar utility to that taught by the present invention.

Godfrey teaches use of the disclosed compounds as fungicides, which is unrelated to the present invention.

(E) Predictability of the technology
The technology in the present case, i.e., anti-cancer therapeutics, is highly unpredictable. Even structurally similar species in the prior art, if any, would be less likely to render a claimed species obvious because it would not be reasonable to infer that they would share similar properties: *In re May*, 574 F.2d 1082 at 1094 (CCPA 1978); *In re Schechter*, 205 F.2d 185 at 191 (CCPA 1953). Unpredictability of the anti-cancer field is exemplified by the present specification itself. For example, the compounds code named BLI-031-2, 0044, and JS-26 each had no detectable anti-proliferative activity (see Example 2, Table 2, at pages 8-9 of the present specification) and yet share with the claimed compounds of claim 26 identical X and Y substituents (see Table 3 at pages 14-17). It is emphasized that none of the prior art disclosed compounds shared common X and Y substituents with the compounds of claim 26. In other words, even with compounds of relatively similar structure (i.e. only 1 substitution group - the Z substituent - being different), the actual anti-cancer activities are very different.

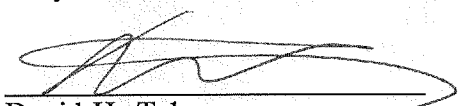
In summary, with respect to Webster et al., four out of the five factors favour a finding of non-obviousness, and with respect to Godfrey all five factors favour a finding of non-

obviousness. With respect to Webster et al., the only factor favouring a finding of obviousness is the teaching of a similar utility. It should be noted however, that Webster et al. teaches a genus of a nearly infinite number of different compounds, and only demonstrates utility with respect to three dithiopyrrolones. As discussed above, the structure of these three disclosed dithiopyrrolones differ significantly from the claimed compounds, and certainly by more than the "very close similar structure" threshold set by the jurisprudence. Moreover and importantly, the anti-cancer field is very unpredictable, as evidenced by the lack of anti-cancer activity of compounds much more similar to the claimed compounds than the three Webster et al. dithiopyrrolones. These other factors are submitted to clearly outweigh the one factor of similar utility.

Given the foregoing, it is submitted that claim 26 (and new claim 28) is patentable over Webster et al. and Godfrey.

The application is submitted to be in condition for allowance, which is respectfully requested.

Respectfully submitted,

By: 

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